constriction of the angioplasty segment between the concentric and eccentric lesion subgroups was not significant (analysis of variance) at any time after PTCA. The degree of vasoconstriction observed in the angioplasty segment of both the concentric and eccentric lesion subgroups were significantly greater than that of the control segment at 15 and 30 minutes after PTCA ($p < 0.01$ and < 0.005, respectively). Figure 4 shows an example of similar spontaneous vasoconstriction after PTCA in 1 patient with a concentric lesion and in a patient with an eccentric lesion.

This study demonstrates that the severity and incidence of spontaneous vasoconstriction in the dilated segment after PTCA does not differ in eccentric versus concentric lesions. On the basis of these findings we would propose that the "release" of the media from the diseased intima after PTCA may restore more normal vasomotor reactivity in concentrically diseased coronary segments. This hypothesis may explain why the vasoconstriction in the treated concentric lesions is equal to that observed in eccentric lesions, which have an arc of relatively disease-free wall. Were it not for this "releasing" effect of PTCA one might expect the vasoconstrictor and vasodilator responses in these concentrically diseased segments to be limited by circumferential atherosclerosis.[10] The ability of intracoronary nitroglycerin to actively vasodilate the angioplasty segment provides further evidence of improved segmental arterial compliance in concentric lesions after PTCA.

Although lesion eccentricity has been regarded as a "risk factor" for complications after PTCA, this study does not support the notion that these complications are attributable to greater vasospasm in eccentric compared with concentric stenoses. However, given the magnitude of the vasoconstrictor responses observed in some of these patients, it is likely that spontaneous vasoconstriction after PTCA does contribute to acute closure syndromes after PTCA of both eccentric and concentric lesions.

Despite prior hypotheses to the contrary, coronary lesion eccentricity does not appear to influence the incidence or severity of spontaneous vasoconstriction in the dilated segment after PTCA.

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Edge Detection Versus Videodensitometry for Quantitative Angiographic Assessment of Directional Coronary Atherectomy

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The immediate efficacy of coronary atherectomy should be established by reproducible quantitative coronary analysis.[1] The term "directional atherectomy" suggests that the device can be selectively directed toward the plaque and that its cutting mechanism is potentially less disruptive on vascular architecture than other angioplasty modalities. As a result of this selectively debulking action, the vessel may assume a more circular configuration, and cross-sectional area measurements obtained by edge detection and videodensitometry should become more comparable. This study was undertaken to determine whether videodensitometry and edge detection were equally acceptable methods in assessing the immediate results after atherectomy since the optimal method has not yet been established. Cineangiograms of 20 patients who underwent directional coro-

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nary atherectomy were analyzed with a computer-based coronary angiographic analysis system. The results of the cross-sectional area derived from contour analysis and videodensitometry were compared before and after directional atherectomy.

From September 1989 through September 1990, 55 patients underwent directional coronary atherectomy at the Thoraxcenter. Patients were selected for atherectomy when an eccentric stenosis was present in a proximal coronary artery. This series consists of the initial 20 atherectomy patients (17 men, 3 women). Edge detection and videodensitometry were used to evaluate the immediate results after atherectomy. All patients underwent a successful procedure without preceding or adjunct balloon angioplasty. Patients ranged in age from 42 to 76 years (mean 62). Coronary angiography showed 1-vessel disease in 14 patients, 2-vessel disease in 3 and 3-vessel disease in 3. The site of the obstruction was located in the left anterior descending coronary artery in 10 patients, the circumflex coronary artery in 2, the right coronary artery in 6 and a coronary artery bypass vein graft in 2.

After administration of local anesthesia, an 11Fr sheath was inserted into the femoral artery. All 20 patients received 250 mg of acetysalicylatic acid and 10,000 U of heparin intravenously. Intracoronary injection of isosorbide dinitrate was performed to relieve any possible spasm. After the initial angiograms in multiple views were completed, a special 11Fr guiding catheter was placed into the ostium of the coronary artery. Under fluoroscopy, the guidewire was advanced into the distal part of the artery; then, the atherectomy device was slipped over the guidewire and positioned across the stenosis. After proper positioning, the support balloon was inflated up to 0.5 atm, the cutter was retracted and balloon inflation pressure was increased to 2 to 3 atm. The driving motor was activated and the rotating cutter was slowly advanced to cut and collect the protruding atherosclerotic lesion in the collecting chamber located at the tip of the catheter. After each pass, the balloon was deflated and either removed or repositioned. On average, 6.7 (3 to 14) passes were performed across a stenosis. Atherectomy was considered successful when the residual stenosis was <50% after tissue retrieval. After atherectomy the arterial and venous sheaths were usually left in place for 6 hours. Patients were monitored for 24 hours, and electrocardiograms and cardiac enzyme levels were obtained twice a day. Nifedipine was administered every 2 hours after the

TABLE I Edge Detection Before and After Directional Atherectomy

	Before Atherectomy	After Atherectomy	p Value
Reference diameter (mm)	3.05 ± 0.55	3.40 ± 0.44	0.05
Obstruction diameter (mm)	1.08 ± 0.43	2.68 ± 0.42	0.000001
Diameter stenosis (%)	66 ± 10	20 ± 9	0.000001

TABLE II Minimal Luminal Cross-Sectional Area Derived from Edge Detection and Videodensitometry Before and After Coronary Atherectomy

	Minimal Cross-Sectional Area (mm^2)					
	Before Atherectomy			After Atherectomy		
Pt. No.	ED	VD	Difference	ED	VD	Difference
1	0.70	0.66	0.04	7.60	5.40	2.20
2	1.00	0.56	0.44	6.70	6.90	−0.2
3	0.40	0.26	0.14	6.20	5.00	1.20
4	0.50	0.16	0.34	7.30	7.30	0.00
5	1.10	1.33	−0.23	10.0	9.06	0.94
6	1.60	1.65	−0.05	6.60	2.99	3.61
7	0.60	0.56	0.04	3.20	2.86	0.34
8	0.92	0.67	0.25	4.81	4.22	0.59
9	0.49	0.25	0.24	4.80	4.19	0.61
10	2.70	3.58	−0.88	6.50	5.72	0.78
11	2.00	1.75	0.25	3.90	5.35	−1.45
12	0.70	0.58	0.12	5.70	6.37	−0.67
13	0.90	0.70	0.20	1.80	1.80	0.00
14	1.8	3.4	−1.6	3.30	3.98	−0.68
15	0.5	−0.42	0.92	7.80	7.23	0.57
16	2.60	2.77	−0.17	6.30	5.50	0.80
17	0.60	0.17	0.43	5.20	4.26	0.94
18	1.2	1.6	−0.40	8.50	10.1	−1.60
19	1.79	1.88	−0.09	5.30	5.20	0.10
20	0.33	0.65	−0.32	6.70	4.79	1.91
		Mean ± SD −0.01 ± 0.52			Mean ± SD 0.48 ± 1.21	

ED = edge detection; SD = standard deviation; VD = videodensitometry.

procedure and the patients were maintained on aspirin for 1 year.

Quantitative analysis of the stenotic coronary segments was performed with the computer-assisted Cardiovascular Angiographic Analysis System that has been described in detail elsewhere.[2–7] *To analyze a coronary arterial segment, a 35-mm cineframe was selected. A region of interest encompassing the arterial segment to be analyzed was electronically digitized (512 × 512 pixels) with a high-fidelity videocamera. Contours of the arterial segments were detected automatically on the basis of the weighted sum of the first and second derivative functions applied to the digitized brightness profile. From these contours, the vessel's diameter functions were determined by computing the shortest distance between the left and right contour positions. A computer-derived estimation of the original arterial dimension at the site of the obstruction was used to define the interpolated reference diameter. This technique is based on a computer-derived estimation of the original diameter values over the analyzed region (assuming there was no disease present) according to the diameter function. Conversion of the diameter measurements of the vessel to absolute values was achieved by using the contrast catheter as a scaling device after correction for pincushion distortion. The minimal cross-sectional area of the narrowed segment and the interpolated percent area stenosis were then derived by assuming a circular model and comparing the observed stenosis dimensions with the reference values. The angiographic analysis was done using the average of multiple matched views with orthogonal projections whenever possible.*

To determine the changes in cross-sectional area of a coronary segment from the density profile within

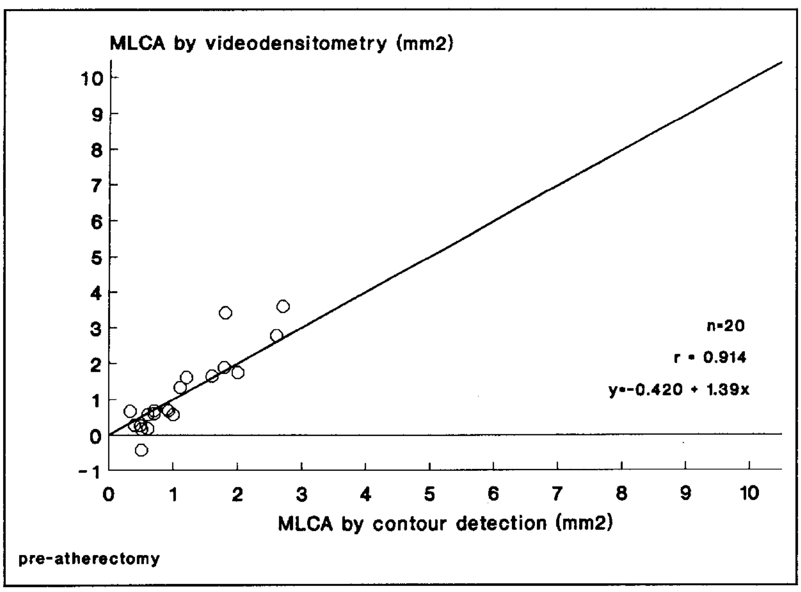

FIGURE 1. Determination of the minimal luminal cross-sectional area (MLCA) by contour detection and videodensitometry before atherectomy. The *line* represents the line of identity. The correlation coefficient is 0.914 (95% confidence interval: 0.791 to 0.966). The regression equation was $y = -0.420 + 1.39x$.

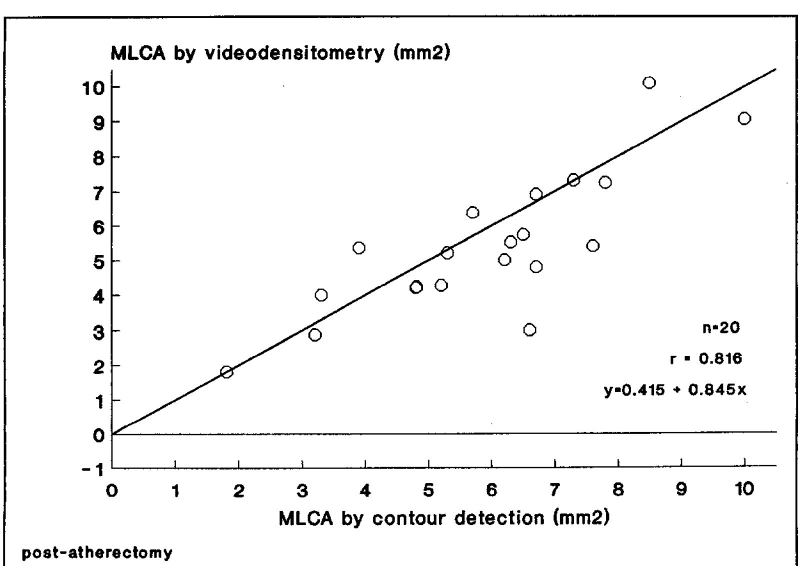

FIGURE 2. Comparison of the minimal luminal cross-sectional area (MLCA) as assessed by contour detection and videodensitometry after atherectomy. The *line* represents the line of identity. After atherectomy a slight deterioration in the relation is found as is expressed by a lower correlation coefficient (0.816). The regression equation was $y = 0.415 + 0.845x$.

the artery, the calibration of the brightness levels in terms of the amount of x-ray absorption (Lambert Beer's law) is required. The videodensitometric method used with our system corrects for spacially variant responses in the imaging chain and for daily variations in the cinefilm processing. Details of this technique have been described elsewhere.[2-7] *Contours of the artery are detected by automated contour detection with the Cardiovascular Angiographic Analysis System, as previously described. Diameter data are derived from the measured diameters along the analyzed segment. On each scan line perpendicular to the centerline of the vessel, a profile of brightness is measured. This profile is transformed into an absorption profile by means of a simple logarithmic transfer function. The background contribution is estimated by computing the linear regression line through the background points directly left and right of the detected contours. Subtraction of this background portion from the absorbed profile within the arterial contours yields the net cross-sectional absorption profile. Integration of this function gives a measure for the cross-sectional area at the particular scan line. By repeating this procedure for all scan lines, the cross-sectional area function is obtained. A reference densitometric area is obtained using the same principles as described for the diameter functions. Calibration of the densitometric area values is accomplished by comparing the reference area calculated from the diameter measurements (assuming a circular cross-section) with the corresponding densitometric area value. The complete procedure has been evaluated with cinefilms of perspex models of coronary obstructions.*[6]

The individual data for diameter and densitometric area measures were used to calculate the mean ± standard deviation. Analysis of variance was performed to compare the area measurements derived from edge detection (assuming a circular cross-section) and densitometry before and after atherectomy, and when significant differences were found, 2-tailed

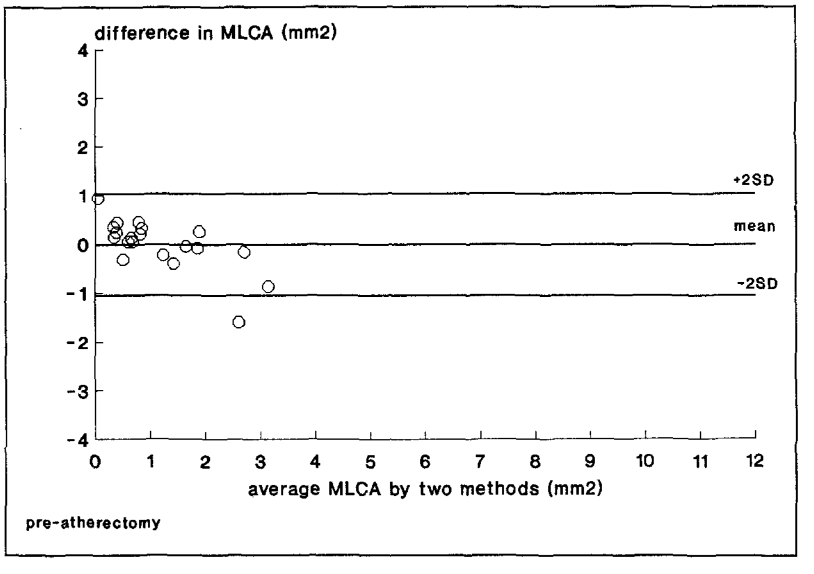

FIGURE 3. Individual data of the average minimal cross-sectional area (MLCA) before atherectomy assessed by edge detection and videodensitometry versus the difference in cross-sectional area between the methods. The mean difference before atherectomy was 0.01 mm^2. SD = standard deviation.

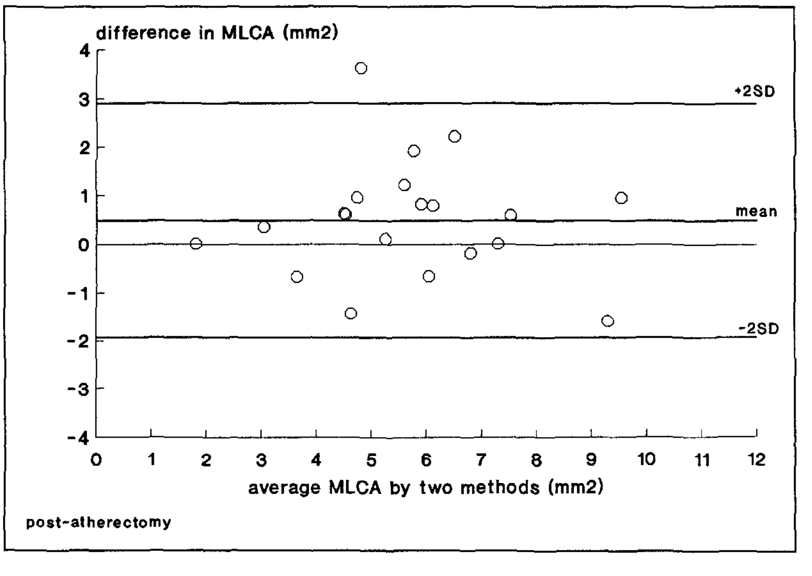

FIGURE 4. Comparison of the average minimal cross-sectional area (MLCA) after atherectomy by edge detection and videodensitometry versus the difference in cross-sectional area between the methods. After atherectomy the difference was slightly higher (0.48 mm^2). The variability was larger after than before atherectomy. SD = standard deviation.

paired t *tests were applied. A statistical probability <0.05 was considered significant. To measure the strength of the relation between the 2 methods of analysis (edge detection and videodensitometry) in the determination of minimal cross-sectional area, the product-moment correlation coefficient (r) and its 95% confidence intervals were calculated at 2 distinct times of study. The agreement between the 2 measures was assessed by determining the mean ± standard deviation of the between-method difference, as suggested by Bland and Altman.*[8] *At each interval, this was done by computing the sum of the individual differences between the 2 methods to determine the mean difference ± standard deviation.*

In this study, the angiographic projection with the severest narrowing was analyzed. The individual data obtained by edge detection and videodensitometry are presented in Tables I and II. On average, the reference diameter increased from 3.1 to 3.4 mm ($p = 0.05$); the obstruction diameter increased from 1.1 to 2.7 mm ($p <0.000001$); thus, the interpolated diameter stenosis was reduced from 66 to 20% ($p <0.000001$). Quantitative analysis of the atherectomy device showed an increase in its diameter from 2.0 ± 0.2 to 3.4 ± 0.4 mm after inflation of the support balloon. The minimal luminal cross-sectional area determined by densitometry was compared with the minimal luminal cross-sectional area measurements from edge detection which assumes a circular configuration. The comparative data before and after coronary atherectomy are shown in Table II and Figures 1 and 2. The minimal luminal cross-sectional area increased after atherectomy from 1.12 ± 0.72 to 5.91 ± 1.95 mm^2 ($p <0.0001$). In patient 15, a coronary artery side branch ran parallel to the stenotic coronary artery and contributed to an increase in the background brightness value. Subtraction of this increased background contribution yielded a negative cross-sectional absorption profile at the site of the coronary artery obstruction. Before atherectomy, the correlation coefficient was 0.914 (95% confidence interval, 0.791 to 0.966), indicating a reasonable linear relationship between the 2 techniques. However, this deteriorated slightly after atherectomy, resulting in a correlation coefficient of 0.816 (95% confidence interval, 0.584 to 0.924). The agreement between the 2 measurements is illustrated in Table II and Figures 3 and 4. The mean difference of the minimal cross-sectional area between the 2 methods before atherectomy was −0.01 mm^2; this difference was slightly larger after atherectomy (mean difference 0.48 mm^2). The variability as determined by the standard deviation of the between-method difference was higher after (1.21 mm^2) than before (0.52 mm^2) atherectomy.

The use of quantitative angiographic analysis for assessing both the immediate and long-term results of interventional techniques appears mandatory. Whether edge detection or videodensitometry should be used as the gold standard continues to be debated. Densitometry has been proposed as an alternative method of quantitative assessment of the severity of coronary artery stenosis. It is based on the linear relation that exists between the optical density of a contrast-enhanced lumen and the absolute dimensions of the arterial segment, and is therefore independent of the geometric shape. Discrepancies between edge detection and videodensitometry are most likely to occur when the shape of the vessel wall at the level of the stenosis deviates furthest from a circular configuration, because it is a basic assumption in the calculation of minimal luminal cross-sectional area by edge detection.[2] Previous studies have shown discrepancies in the analysis between edge detection and videodensitometry after balloon angioplasty.[2] Since the cutting mechanism of atherectomy is expected to remodel the treated coronary artery into a more concentric and circular configuration, densitometry should correlate closely with the cross-sectional area measurements derived from edge detection.

Because comparing 2 methods in clinical practice should not only be limited to the assessment of the strength of the relation (correlation coefficient, r),[8] we also included the assessment of the degree of agreement or variability, which is determined by the mean ± standard deviation of the between-method difference. This comparative study illustrates that a linear relation exists between the 2 methods both before and after atherectomy. However, it must be emphasized that the strength of the relation deteriorates slightly after atherectomy. Overall, a good agreement exists between the 2 methods, although edge detection slightly underestimates the minimal luminal cross-sectional area before atherectomy and overestimates the minimal cross-sectional area after atherectomy.

Quantitative coronary angiography shows that a similar discrepancy exists in the postatherectomy analysis between edge detection and videodensitometry when compared with the results in a previous balloon angioplasty study.[2] This observation suggests that edge detection and videodensitometry are equally acceptable methods for assessing the results of interventional techniques, although small differences exist in the postinterventional analysis. The possible explanation for these differences is the occurrence of trauma to the vessel wall by the interventional devices. This obviously results in the formation of intimal flaps and dissections with subsequent distortion of the vessel configuration. The recoil phenomenon, as assessed after balloon angioplasty, may also play an important role.[9] Stent implantation apparently counteracts these influences by acting as a scaffolding device and by its self-expanding property.[10,11] This suggests that the cutting mechanism of atherectomy and the barotrauma of balloon angioplasty result in similar eccentric vessel contours.

In conclusion, despite small differences in minimal luminal cross-sectional area after intervention, edge detection and videodensitometry are equally acceptable methods in assessing the immediate results after atherectomy. Atherectomy, as well as balloon angioplasty, induce substantial trauma to the vessel wall, which results in a noncircular vessel configuration. The smoothing process of stenting results in more circular vessel contours compared with balloon angioplasty and atherectomy.

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Effects of Parasympathetic Blockade on Ischemic Threshold in Patients with Exercise-Induced Myocardial Ischemia

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In patients with coronary artery disease (CAD), an abnormal coronary vasoconstriction superimposed to organic stenosis may further limit coronary flow reserve.[1] This functional factor can modulate flow availability to the ischemic region and be responsible for the variability of ischemic threshold frequently observed in patients with effort angina pectoris.[2] An imbalance between dilatatory and constrictor stimuli has been postulated in these patients, possibly related to the impairment of the endothelium-mediated regulation of smooth muscle tone.[3] In normal subjects, coronary infusion of acetylcholine produces coronary vasodilation that appears to be mediated by the endothelium-derived relaxing factors, whereas in patients with CAD, it reduces large coronary artery diameter and decreases coronary flow velocity[4] (in animal experiments this latter effect seems to be independent of both α and β blockade, and is promptly reversed by intravenous injection of atropine).[5]

A similar phenomenon can be observed during exercise. Compared with normal subjects, patients with CAD have a paradoxical vasoconstriction of large epicardial coronary arteries that can be prevented by treatment with isosorbide dinitrate.[6,7] It can be hypothesized that in normal conditions the parasympathetic system opposes vasoconstriction during exercise, whereas in the absence of endothelium its effect is reversed to coronary vasoconstriction. The aim of this study was to evaluate the effect of atropine, a parasympathetic blocker, compared with that of isosorbide dinitrate, an endothelial independent vasodilating drug, on the ischemic threshold of patients with exercise-induced ischemia.

Seventeen of 23 consecutive patients (14 men and 3 women, mean age ± standard deviation 54 ± 4 years) with history of effort angina of unchanged severity in the preceding 3 months, typical exercise-induced ST-segment depression and angiographically documented CAD gave informed consent to enter this study.

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